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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/423,546	04/25/00	BENNETT-GUERRERO E	08213/007001

HM22/0927

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EXAMINER	
SWARTZ,R	
ART UNIT	PAPER NUMBER
1645	13

DATE MAILED: 09/27/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trad marks

Office Action Summary

Application No.	Applicant(s)
09/423,546	Bennett-Guerrero et al
Examiner	**Art Unit**
Rodney P. Swartz, Ph.D.	1645

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on 25April2000 .

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) 44-100 is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☐ Claim(s) _____ is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☒ Claims 44-100 are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)

16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 4, 11

18) ☐ Interview Summary (PTO-413) Paper No(s). _____

19) ☐ Notice of Informal Patent Application (PTO-152)

20) ☐ Other:

DETAILED ACTION

1. Applicants' Preliminary Amendment, received 25April2000, paper#9, is acknowledged. Claims 1-43 have been canceled. New claims 44-100 have been added.

2. Currently, claims 44-100 are pending and under consideration.

Drawings

3. The formal drawings submitted with the application have been reviewed by the Draftperson and have been approved.

Information Disclosure Statements

4. Upon examination of the application, the examiner has discovered three Information Disclosure Statesments, but only references for one of the statements.

PTO-1449, 2 pages of listings --- no references provided

PTO-1449, received 6March2000 --- references provided

PTO-1449, received 13October2000, 13 pages of listings --- no references provided

A clarification is required.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to

make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claim 45 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 45 recites that the LPS atigen is from ≥ two of the listed bacteria. However, *Salmonella* and *Bacteroides* are listed as one choice, not as two separate bacteria. It is unclear if a semicolon is missing following *Salmonella* or if the two bacteria are to be considered as one bacteria.

8. Claims 45-100 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 44 recites "a composition comprising rough, complete-core lipopolysaccharide(LPS) antigen of a gram negative bacterium". The use of "a gram negative bacterium" denotes a singular bacterium source.

The dependent claims all recite that the composition of claim 44 "comprises" more bacteria, i.e., plural sources. The dependent claims do not recite that the composition of claim 44

"further comprises". Therefore, it is unclear what are the component(s) of the compositions in the dependent claims.

9. Claims 44-96, 99-100 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for producing antibodies by immunizing with compositions comprising rough complete-core LPS, does not reasonably provide enablement for treatment of animals by reducing the adverse effects of endotoxin. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Enablement requires that the specification teach those in the art to make and use the invention without undue experimentation. Factors to be considered in determining whether a disclosure would require undue experimentation include (1) the nature of the invention, (2) the state of the prior art, (3) the predictability or lack thereof in the art, (4) the amount of direction or guidance present, (5) the presence or absence of working examples, (6) the quantity of experimentation necessary, (7) the relative skill of those in the art, and (8) the breadth of the claims.

The nature of the invention - methods of reducing the adverse effects of endotoxin in warm blooded animals, i.e., *in vivo* treatment, comprising administration of a composition comprising rough, complete-core LPS.

The state of the prior art - high concerning immunization with gram negative bacteria.

The amount of direction or guidance present - While the instant specification discusses the adverse effects which are imparted by endotoxin and the structure of smooth and rough core LPS, the specification is silent concerning examples of the treatment of animals to reduce the adverse effects of endotoxin. The specification teaches antibody production and *in vitro* binding assays. The specification no examples concerning the dosage, timing of administration, etc. which are the necessary parameters for determining the proper steps to fulfill the methods claimed.

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. Claims 44, 45, 47-49, 59, 60, 61, 62, 63, 64, 66-69, 72-76, 84-89, 93, 95-100 are rejected under 35 U.S.C. 103(a) as being unpatentable over Johns et al (*Inf. Immun.*, 17(1):9-15, 1977) in view of Gram et al (U.S. Pat. No. 5,858,728).

The instant claims are drawn to a method of reducing adverse effects of endotoxin in an animal comprising administration of an effective amount of a composition comprising rough,complete-core lipopolysaccharide antigen of a gram negative bacterium.

The open language, "a composition comprising", encompasses not only isolated/purified LPS, but whole mutant bacteria which "comprise" or contain the LPS.

Johns et al teach the administration of rough mutants *S. minnesota* Ra, Rb, Rd, and Re to animals, producing antibodies which bind to the core LPS (section *Materials and Methods*) and teach that such administration is protective (page 15, 3rd paragraph, first column). Johns et al do not teach monoclonal antibodies or reducing endotoxic effects.

Gram et al teach that monoclonal antibodies produced against such LPS from rough complete core mutants of *E. coli*, and *Salmonella* passively cross-protects against endotoxemia (Abstract; col. 3, lines 3-52; Example 1).

Therefore, it would have been obvious to one having ordinary skill in the art to modify the teachings of Johns et al and Gram et al to directly administer the rough, complete-core LPS mutants to protect against endotoxemia in recipients.

Conclusion

12. No claims are allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rodney P. Swartz, Ph.D., whose telephone number is (703) 308-4244. The examiner can normally be reached on Monday through Friday from 6:30 AM to 4:00 PM EST.

If attempts to reach the Examiner by telephone are unsuccessful, the examiner's supervisor, Lynette F. Smith, can be reached on (703)308-3909. The facsimile telephone number for the Art Unit Group is (703)308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the group receptionist whose telephone number is (703)308-0196.

RODNEY P SWARTZ, PH.D
PRIMARY EXAMINER
Art Unit 1645

September 27, 2001